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## DISCUSSION

HOWARD O. BALL, M. D. (The W. K. Kellogg Foundation, Los Angeles).—This paper points out very aptly many of the difficult and only partially solved problems connected with the study of malignant tumors, clinically or experimentally. The questions of *how* and *why* for even the observations presented here remain largely unanswered. Species specificity for transplantable tumors is no longer specific. German workers have recently recorded the transplantation of a human tumor (carcinoma of cervix) to white mice.

I heartily agree with Doctor Connor that a great need for fundamental laboratory work exists; and an important field, I think, is chemistry. We need more specific reactions for organic substances when present in small amounts in tissues or body fluids. We need histochemical reactions in the microscopic study of cancer tissues, and cancer cells. The explanation of many of the problems of the transmissibility, and possibly even of the hereditary susceptibility of malignant tumors, may finally be chemical. Such a knowledge would help us better to interpret the exceptions which exist. It would certainly indicate whether malignant diseases should be considered as having a common etiology, and thus whether any single procedure could ever be reasonably expected to modify the course or exterminate the existence of a malignant process.

Every present-day method of treating malignant diseases is empirical. Rational therapy can only follow more knowledge of a fundamental character, particularly as regards etiology.

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H. J. ULLMANN, M. D. (Santa Barbara Cottage Hospital, Santa Barbara).—Doctor Connor's paper when published will be of great value as a reference work to all those doing research in cancer. It should be read by all surgeons, radiologists, and clinicians, who are dealing with cancer, so that they may think with knowledge and not become too enthusiastic over the regression of a few tumors following the use of any new method of treatment. It is only by the observation of large numbers of tumors in comparison with controls that any method of treatment can be properly evaluated. I was much interested in the suggestion that the increased necrosis or a liquefaction of some tumors following the injection of various substances might be due to an acceleration of growth with choking off of the blood supply, rather than a direct effect on the tumor tissue itself. This is undoubtedly a factor or possibility that must be taken into consideration. We have lately been able to study such effects. Bischoff and Maxwell, in our laboratories, have found that the Allan-Doisy follicular preparation, corpus luteum extract, and four adrenal extracts, when injected subcutaneously into rats, brought about an early instance of liquefaction or opening of R-10 sarcoma without effecting the incidence of regression.

I do not believe it possible, on the basis of our present knowledge of cancer, that any single substance or method of treatment will ever be found that may be used for all types of malignancy. To me it is as absurd to look for a single cancer cure or treatment as it is to look for a single cure or treatment for "infectious disease." And the treatment of all

forms of malignancy by one method is equivalent to treating such infections as malaria, syphilis, and pneumonic plague, with the same remedies and procedures.

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W. T. CUMMINS, M. D. (Southern Pacific General Hospital, San Francisco).—The world's major medical subject appears undeniably to be a biochemical problem. Each of the main types of spontaneously developing malignant tumors may be caused by a specific, and possibly widely different, pathologic metabolic product, or group of products. The subject of immunity and susceptibility in lower animals, as well as in human beings, is as conspicuous in the problem of neoplastic study as it is in infectious diseases. Spontaneous retrogression and disappearance of neoplasms and their retrogression, in consequence of protein inoculation, are subjects of great interest.

Exhaustive studies of histochemical conditions in normal, abnormal non-neoplastic and neoplastic tissues may illuminate the subject. This work is being carried out apparently by a very limited number of investigators.

The topic presented by Doctor Connor has been elaborated most interestingly and well, with the presentation of the facts and of the problems that confront the investigator.

To the progressively increasing army of workers throughout the world, there must be added a host, all of whom, well trained, must attack the neoplastic problem for its final subjugation.

## TRICHORRHEXIS NODOSA—A CLINICAL PROBLEM\*

## REPORT OF CASES

By CHARLES R. CASKEY, M. D.  
Los Angeles

DISCUSSION by Stanley O. Chambers, M. D., Los Angeles; Hiram E. Miller, M. D., San Francisco; H. J. Templeton, M. D., Oakland.

IT was with considerable hesitancy that I decided to write upon a subject about which so little is known. However, having observed twelve cases of a supposedly rare condition during the past year and having made some observations on the course and treatment of a few of them, I deem it worth while to report these cases at this time. If this incomplete report stimulates further study its aim will have been attained.

In order to obviate any confusion that may exist on the part of my hearers concerning the nomenclature of the subject of this essay, the following terms are defined: Trichorrhesis nodosa, as the name implies, is characterized by the presence on the shaft of the hair of one or more irregularly spaced, small, grayish nodes. Microscopically, these nodes at that point show longitudinal splitting of the hair, resembling two small paint brushes jammed end to end. Trichoclasia, essentially a later stage of trichorrhesis nodosa, is the transverse fracture of the shaft of the hair at the middle of the node from traction or bending, while trichoptilosis designates a longitudinal splitting of the shaft of the hair into two or more fibrils.

\* Read before the Dermatology and Syphilology Section of the California Medical Association at the fifty-ninth annual session at Del Monte, April 28 to May 1, 1930.

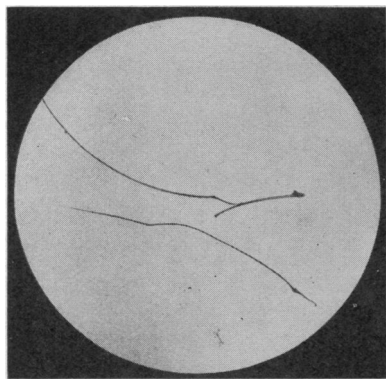


Fig. 1.—Hair stubs from Case 1. Both are small and poorly nourished hairs. Note the nodes near the bulb in each stub. The upper hair illustrates trichoclasia. Transverse fracture of the node is almost complete. The stubs were removed with very little traction. This shows definitely the connection between trichorrhexis nodosa and the loss of hair in this case. These stubs were obtained only after careful and close search of the affected portion of the scalp and were the last affected hairs found. Ordinarily they would have been removed by combing, washing, or brushing.

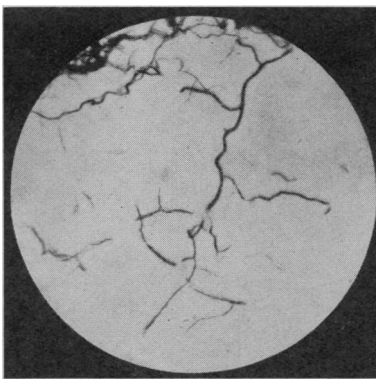


Fig. 2.—Photomicrograph of organism in Case 2. Culture six days old. Branched mycelia and beginning spore formation shown.

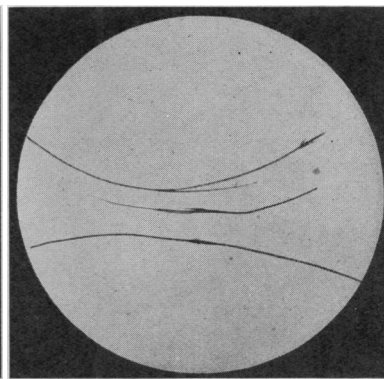


Fig. 3.—Trichorrhexis nodosa (two lower hairs). Trichoptilosis (upper hair). From Case 3.

#### CAUSATIVE ORGANISM

As recently as 1928 Marcoglou reviewed the literature to date; hence, further comment in this contribution seems unnecessary. Marcoglou reported negative cultures and drew no conclusion as to the etiology.

In reporting this small series of cases, I wish to call attention to the cultural findings in two of them. While this percentage is small, it approaches the findings in other bacteriological tests. We do not know why some organisms are difficult to cultivate on artificial media; we theorize that the media do not approach the soil from which the organism was taken. In theorizing, in the case of trichorrhexis nodosa, it is possible that the organism here cultured gains entrance into the hair shaft within the moist portion of the follicle and there begins to disintegrate the hair while it is growing upward, the fungus gradually dying after the hair grows beyond the moist portion of the scalp. In this way a noded or split hair that had grown out some distance, if taken for culture, would be less likely to produce a growth. Material used for culture in this investigation was taken at random. Some of the diseased hairs were plucked out and others just cut off and planted. This fact was not noted when the records of plantings were made. Some cultures did not produce a positive growth on the first or second planting. Four to eight affected hairs were planted in each culture tube. The value of multiple plants teaches us that we should not, as in all fungus studies in particular, give up the direct search or cultural test until after many trials have been made. Think of the persistence of Castellani, who examined for nineteen consecutive days the scrapings from a single case of pruritus ani before finding the causative

organism. It is a well known fact that clinically positive dermomycosis frequently offers negative direct and cultural evidence of causative organisms. I believe figures have been established to show that such failure occurs in 50 per cent of attempts, although repeated examinations raise the incidence markedly.

#### REPORT OF CASES

CASE 1.—P. S., a male, age twenty years, came to the clinic complaining of loss of hair in the parietal regions. A tentative diagnosis of alopecia prematura was made. There was no definite bald area, but a general thinning and shortening of the hair on each side. It looked like the beginning of hair loss which terminates in the typical bald head. In this case the loss of hair was rather sudden and confined, at first, to the left frontoparietal area where for a time many hairs which were only loosely attached could be removed by gentle traction. In a week the right frontoparietal area was noticeably thin. There was no evidence of pityriasis sicca, oleosa, or a true seborrheic dermatitis, and the scalp was apparently in a healthy condition. The patient gave a history of not wearing a hat for several years except now and then on special occasions. His care of the scalp consisted of a soap and water shampoo every two weeks. He had not been using any tonics or barber-shop preparations. A tonic was prescribed but did not seem very efficacious. He complained that his hair was splitting and breaking off. Not much attention was paid to this complaint at first, but I promised that if he would bring some combings I would examine some of the hairs under the microscope. Typical trichor-

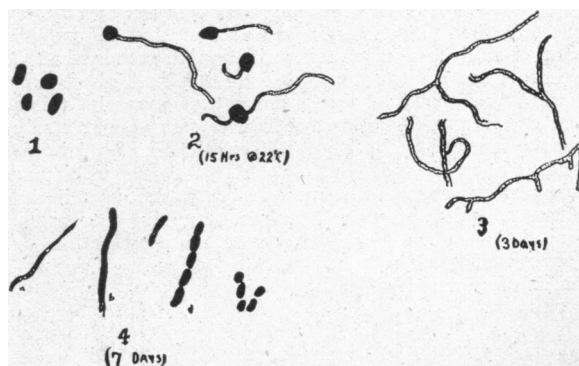


Fig. 4.—Drawing of organism in Case 2, showing life cycle from spore through mycelia formation back to the spore stage. (By courtesy of Dr. Robert A. Stewart, University of California, Department of Bacteriology.)

rhexis nodosa and trichoptilosis were found in this sample. To the unaided eye no hairs back of the center of the scalp were affected, and at no time during my observation of this case could diseased hairs be found on the scalp except in the above mentioned areas.

After numerous plantings of noded and split hairs, a growth appeared which will be described later. At one time a number of hair stubs were planted which gave a good growth after two weeks. The stubs almost disappeared. What were left were soft and broke up easily when pressed out on a slide. This is the best evidence I have that the organism feeds on and destroys the hair. This patient is still under observation. No affected hairs have been found on the scalp for three months and the hair has grown thicker. With the disappearance of the trichorrhexis nodosa the alopecia has improved.

The treatment in this case was as follows. The entire scalp was shaved and ultra-violet light treatments were given every week or two. For a time, at night, biweekly inunctions of the scalp with an ointment containing two per cent salicylic acid and three per cent sulphur was used. This was shampooed out with tar soap the next morning. A euresol, bichlorid, and salicylic acid lotion was used each morning. Fowler's solution was given internally. Most of the time the patient wore no hat and the hair was kept clipped short. The result has been an arrest of the falling of hair and a partial regrowth.

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CASE 2.—D. M., a girl, age thirteen years, came with the complaint of loss of hair of a month's duration. The history, as told, was that the onset appeared as a small crusted spot on the top of the head which seemed to disappear with the application of tincture of iodine. After this the hair came out rather rapidly. The patient was well nourished and in good health. This case presented a large spot of thinned hair on the vertex of the scalp about five or six inches in diameter. In places there was evidence of a new growth of hair. There was no evidence of pityriasis sicca, oleosa, or seborrheic dermatitis anywhere on the scalp.

Unfortunately this patient made only one call at the office, but luckily two plants of the affected hairs were made on Sabouraud's glucose media, the results of which will be referred to later.

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CASE 3.—Mrs. R. H., age thirty-four, did not come in on account of a hair condition. She states, however, that her hair comes out rather freely when combed. Two independent cultural studies carried out in this case from material taken on different dates

yielded an identical *Nocardia*-like fungus. The organism has not yet been submitted to a mycologist for definite classification. Its life cycle is a little more rapid than that of Cases 1 and 2, and it is somewhat smaller in size. Cultural and microscopic appearances, however, are very much like those of the other two cases. This emphasizes the fact that similar, though not necessarily identical, organisms may produce the same final gross pathology.

#### CULTURAL STUDIES

Cultural studies were carried out by planting the affected hairs, four to eight to a single slant, on Sabouraud's glucose media. Several slants were made if material was available. The tubes were kept at room temperature in an upright position and in a place where some light was available.

The growth of the organism in these two cases was slow. A transplant will cover one-third of the surface of an agar slant in one month. It will grow at room temperature, but its optimum growth is at 37 degrees Centigrade. On Sabouraud or glucose agar a dry, compact, white, powdery surface growth is produced. As the growth becomes older there is some crumpling of the media. A distinct earthy odor is apparent when an old tube is opened. The organism does not ferment lactose, sucrose, maltose, mannite, glucose, levulose, galactose, glycerol, raffinose, or zylose. It does liquefy gelatin and gives a grayish white rugose growth on potato. It would not grow in the absence of free oxygen. Inoculation into the skin of a guinea pig was negative, although a small reddish nodule persisted for three days without marked inflammation and disappeared completely in about a week.

Cultural material was examined microscopically with the following findings. The fungus is a very small organism and requires an oil-immersion lens to study it. Like the *Nocardia* group, it appears as a chain of bacteria. It shows distinct branching and forms numerous spores. It is Gram-positive.

According to Castellani's classification this organism belongs to the order Microsiphonales, family Nocardiacae and in the genus *Nocardia*.

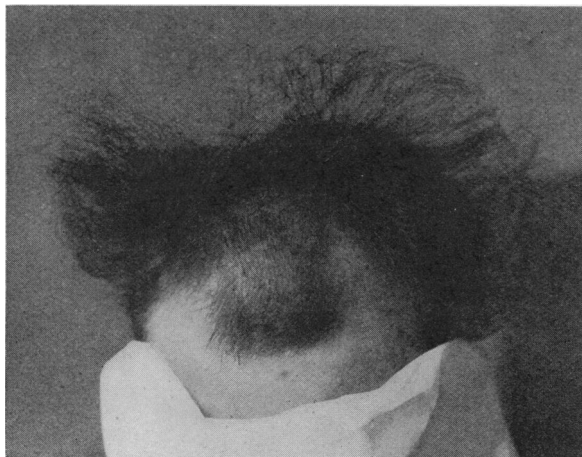


Fig. 5 (Case 1).—Taken at beginning of treatment.

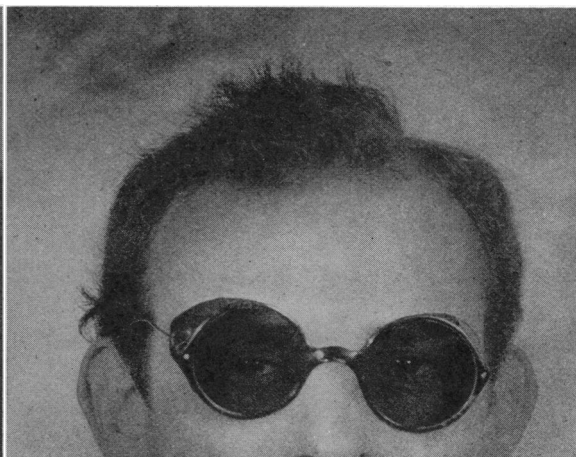


Fig. 6 (Case 1).—Six months after instituting treatment.

## OBSERVATIONS OF TEN OTHER CASES

I have observed this condition, trichorrhexis nodosa, in ten other cases, which are not included in this report since I was unable to carry the cultural tests to completion. Most of these cases sought treatment for some form of hair trouble. In three cases of alopecia areata this nodose condition was discovered in near-by hairs. The finding of these twelve cases of trichorrhexis nodosa during the past year leads me to believe that this supposedly rare condition is, on the contrary, rather frequent and that all cases of hair affections should be examined carefully in good daylight. I am sure if you will do this, you will find, as I have found, many cases of this affection in the future.

These studies have led me to believe that trichorrhexis nodosa may be a low-grade infection, causing very little follicular reaction or defense and as a consequence gradual loss of hair. I am aware, however, of the fact that I have not proved that this fungus which we have isolated and described is the etiological factor in trichorrhexis nodosa. It may have just been an accidental contamination of the hair. It is so small that it was not possible in this study to definitely stain it within the hair and thus demonstrate its presence, although at times I thought I could see it in the unstained hairs. Hence, I have not been able to prove to my satisfaction the pathogenicity of the fungus for the hair. In one of my tests, I planted normal sterile hairs on media and among them a culture of the organism. I was elated when I thought that the sterile hairs had become affected, but spoiled them by softening in hydrate solution in an attempt to stain them. When I repeated the test I was not so sure of my previous findings.

In closing I wish to state that I draw no definite conclusions from these preliminary studies in a few cases. It has just been a small endeavor on my part to settle the etiology in a still obscure condition of the hair. I am desirous of knowing whether this is an etiological entity and what part it plays in the alopecia group, the etiology and treatment of which are very unsatisfactory. Until the etiology of any disease is known there can be no sound therapy.

1930 Wilshire Boulevard.

Note.—For assistance in the isolation and identification of the organism in these studies, I am indebted to Dr. Robert A. Stewart of the department of bacteriology of the University of California at Berkeley, to Dr. W. W. Reich of the department of bacteriology of Stanford University, and to Dr. Roy Hammock of Los Angeles.

## DISCUSSION

STANLEY O. CHAMBERS, M.D. (1260 Roosevelt Building, Los Angeles).—Such investigations as these by Doctor Caskey are exceedingly commendable and should add impetus to further laboratory research in this group of dermatoses. The isolation of an organism from pathological tissues is not *ipso facto* evidence of causation. Its consistent demonstration is, however, highly suggestive. The final requirement is the fulfillment of Koch's postulates, and it is to be

hoped that Doctor Caskey will be as successful in this as he has been in the investigation as far as he has gone.

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HIRAM E. MILLER, M.D. (384 Post Street, San Francisco).—The cause of trichorrhexis nodosa has been a subject of discussion ever since it was first described by Wilson in 1849. The disorder is generally attributed to parasitic, mechanical, or nutritional causes. Bacteria have been isolated by numerous observers, but as far as I know this is the first time that a fungus has been recovered. This investigation has been of considerable interest, and we will all be interested in the complete and final report. In the meantime we must still consider that the fractures or nodes are the result of mechanical injury to a hair probably with a damaged nutrition and associated with heredity.

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H. J. TEMPLETON, M.D. (3115 Webster Street, Oakland).—Doctor Caskey's commendable work has not, as he states, definitely proved that a fungus is the cause of trichorrhexis nodosa. His positive results should stimulate him and others to undertake further studies along this line. One obstacle in his path is that of gathering sufficient clinical material, inasmuch as this condition is a rare one. We could help him if we would send him hairs extracted from any such patients we might see.

I would like to further emphasize Doctor Caskey's statement that one should make many plants of suspected material upon culture media when searching for fungi. In our work on epidermophytosis which is being done at the University of California, Lee Bonar has demonstrated that the proportion of positive findings is not only in proportion to the number of inoculations upon the culture medium but is much higher. Thus, if we increase the number of plantings by a certain per cent the percentage of positive findings increases not only to the same figure, but up to one considerably higher.

Inasmuch as Doctor Caskey is searching for fungi whose natural or acquired habitat is the scalp, I might suggest that he try special culture media such as have been used in searching for another scalp fungus, the pityrosporon of Malassez.

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DOCTOR CASKEY (Closing).—Doctor Lindsay asked if I had observed trichorrhexis nodosa in blonds. I have recently found two cases of the condition in light-haired individuals and do not think color of hair makes any difference in the incidence of this disease.

I agree with Doctor Chambers that it would be more conclusive if Koch's postulates could be carried out in such researches, but do not regard them as a final requirement. Koch's law has not been proved in the case of *Hansen's bacillus*, although this organism has been generally accepted as the cause of leprosy.

As Doctor Miller intimates, it will take further research to prove which of the theories, parasitic, mechanical or nutritional, is operative in bringing about this condition.

I am very glad to have Doctor Templeton emphasize the necessity for making numerous cultural tests in searching for microorganisms in diseases of the skin. One is inclined to become discouraged if the first few attempts are negative. However, we should remember that frequently the pathologist makes many examinations of sputum before giving a negative report in suspected tuberculosis. I am also pleased to have him suggest a special culture media for future use.